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(54) Title: APPARATUS AND METHODS OF BIOELECTRICAL IMPEDANCE ANALYSIS OF BLOOD FLOW			
(57) Abstract			
<p>Apparatus and methods are provided for monitoring cardiac output using bioelectrical impedance techniques in which first and second electrodes are placed in the trachea (103) and/or bronchus (104a) in the vicinity of the ascending aorta (101a), while an excitation current is injected into the thorax (100) via first and second current electrodes (13), so that bioelectrical impedance measurements based on the voltage drop sensed by the first and second electrodes reflect voltage changes induced primarily by blood flow dynamics, rather than respiratory or non-cardiac related physiological effects. Additionally sense electrodes (12) may be provided, either internally, or externally, for which bioelectrical impedance values may be obtained. Methods are provided for computing cardiac output from bioelectrical impedance values. Apparatus and methods are also provided so that the measured cardiac output may be used to control administration of intravenous fluids to an organism or to optimize a heart rate controlled by a pacemaker.</p>			

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APPARATUS AND METHODS OF BIOELECTRICAL
IMPEDANCE ANALYSIS OF BLOOD FLOW

5 Field Of The Invention

 The present invention relates generally to
apparatus and methods for non-invasively measuring
cardiac output and, more particularly, to apparatus and
10 methods for measuring cardiac output using
bioelectrical impedance analysis techniques.

Background Of The Invention

15 Knowledge of cardiac output is crucial in the
care of critically ill patients, as well as patients
with chronic heart disease requiring monitoring of
medication. For many years the standard of cardiac
output measurement has been pulmonary artery
20 catheterization. Previously known catheterization
techniques, as described, for example, in U.S. Patent
Nos. 3,915,155, 3,726,269 and 3,651,318, involve
periodic injection into the patient's bloodstream of a
bolus of heated saline, during which thermodilution
25 measurements are performed to determine cardiac output.
Such techniques cannot generally be used for continuous
monitoring. Moreover, such catheterization techniques
pose significant risk to the patient, including

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5 malignant arrhythmias, pulmonary artery rupture, and in rare cases, death.

Consequently, for many years work has been underway to develop less invasive apparatus and methods for monitoring cardiac output. For example, as an
10 alternative to catheterization methods, Doppler ultrasound techniques have been adapted to measure the velocity of blood flow. If the diameter of a vessel, its flow profile, and the angle of the ultrasound beam relative to the vessel can be determined, Doppler
15 ultrasound measurements of the ascending aorta, either externally (from the suprasternal notch) or internally (from within the trachea) can be used as a measure of cardiac output.

U.S. Patent 4,671,295 describes an example of
20 such methods and apparatus, wherein an ultrasound transducer is mounted on the tip of an endotracheal tube so that Doppler measurements of blood flow from a point (pulse wave mode) or path (continuous wave mode) along the ultrasound beam can be measured. The method
25 described in the patent requires multiple measurements within the blood vessel, a priori knowledge of the blood flow pattern and cross-sectional area of the vessel, and the relative angulation of the blood vessel. In addition, the measurement is highly
30 dependent upon the exact placement of the transducer. These drawbacks have resulted in the slow adoption of Doppler ultrasound cardiac output techniques.

A yet further technique which the prior art has sought to apply to the measurement of cardiac
35 output is bioelectrical impedance analysis ("BIA"). BIA has recently gained wide use as a method for measuring body composition and physiological metrics. BIA involves passing a low level electrical alternating current ("AC") through body tissues between multiple

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5 electrodes, measuring the voltage difference between multiple locations on the tissue, and then calculating the electrical impedance (electrical resistance plus reactance) of the stimulated tissue.

Generally, BIA apparatus employ two current
10 electrodes to conduct a low level excitation current through body tissue. As current flows in the tissue, a potential difference develops across the tissue which is proportional to the value of the AC current and the tissue impedance. The tissue impedance may be
15 calculated by disposing two sense electrodes between the current electrodes and measuring the voltage difference between the two sense electrodes.

Current flows predominantly through body materials with high conductivity, such as blood. Less
20 current flows through muscle, which has an intermediate conductivity, while the conductivity of fat, air and bone is much lower than that of either blood or muscle. Because the resistance to current flow is a function of the conductivity and cross-sectional area of the
25 conducting volume, volumes having a larger cross-sectional area have lower electrical resistance.

It is also known that the impedance of the conducting volume and the measured medium metrics (i.e., static parameters such as fat or water content,
30 and dynamic metrics, such as blood flow) are dependent upon the placement of the electrodes and the conducting path between the electrodes. Thus, the greater the distance between the electrodes, the more likely that extraneous variables will affect the measurement.

35 Previously known BIA methods generally correlate the measured voltage drop between the sense electrodes to tissue impedance using relatively simple algorithms based on simplified models of body structure, for example, by assuming that the body is

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5 composed of simple cylindrical resistive volumes.
Temporal cyclical variations in the body impedance are
then assumed to result from physiological events such
as blood flow and breathing.

10 Measurements of the electrical impedance, and
particularly, the time-varying nature of electrical
impedance, may therefore provide a non-invasive
indicator of physiological events. Various algorithms
have been developed to isolate specific physiological
15 parameters, such as cardiac output, from the measured
bioelectrical impedance, as described, for example, in
W.G. Kubicek, et al., "Development And Evaluation Of An
Impedance Cardiac Output System," Aerospace Medicine,
Vol. 37, pp. 1208-1212 (1966) and U.S. Patent No.
3,340,862, which is incorporated herein by reference.

20 Despite the application of BIA methods for
measuring cardiac output, no simple continuous BIA -
based cardiac output measurement device has gained
widespread acceptance. Many existing BIA devices use
external or internal electrodes to measure
25 bioelectrical impedance for large volumes, for example,
the whole body or thoracic segments. Because the
excitation current diffuses throughout the entire
volume, making use of any and all conductive paths,
differences between individual patients, and even for
30 the same patient over time, may inhibit standardizing
the BIA metrics.

Moreover, it is known that while BIA
measurements of cardiac output provide good correlation
for normal patients and those hemodynamically stable
35 patients, there is poorer correlation for critically
ill patients and patients in heart failure, as
described, for example, in R.J. Detemeter et al., "The
Use Of Noninvasive Bioelectric Impedance To Determine

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5 Cardiac Output: Factors Affecting Its Accuracy," Am. J. Noninvasive Cardiol., Vol. 2, pp. 112-118 (1988).

 An example of an attempt to overcome the variabilities encountered when taking bioelectrical impedance measurements across large volumes is
10 described, for example, in U.S. Patent No. 4,870,578. That patent describes BIA apparatus for monitoring cardiac output by using external electrodes that measure the electrical resistance of a segment of the thorax and includes circuitry to account for
15 respiratory-induced voltage changes. As acknowledged in that patent, the respiratory-induced voltage changes are typically much greater than the cardiac-induced voltage changes.

 Other devices that attempt to account for the
20 effect of non-cardiac physiological events on bioelectrical impedance include arranging multiple electrodes on esophageal catheters to measure thoracic bioelectric impedance, as described, for example, in U.S. Patent Nos. 4,852,580 and 4,836,214. Both patents
25 describe multi-electrode arrays inserted into the esophagus to provide an impedance measurement reflecting blood flow in the descending aorta. Such devices are not believed to provide true isolation of cardiac-induced voltage changes from those induced by
30 other physiological events. In addition, these systems do not ensure that the multiple electrodes make positive contact with the esophageal wall.

 BIA measurements have also been employed to provide a metric of cardiac output by measuring
35 physiologic effects other than blood flow. For example, U.S. Patent No. 4,953,556 describes a BIA arrangement including an internal electrode mounted on an esophageal catheter and an external electrode which is disposed above the apex of the heart. The apparatus

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5 described in that patent attempts to use BIA
measurements to determine cardiac wall motion and lung
motion, from which an estimate of cardiac output and
pulmonary activity can be obtained.

10 In view of the foregoing, it would be
desirable to provide apparatus and methods for
accurately, non-invasively and continuously measuring
cardiac output using BIA techniques.

15 It further would be desirable to provide
apparatus and methods for measuring cardiac output in
critically ill patients using BIA techniques that
overcome the inaccuracies arising from measuring
voltage changes across whole body or large volume
thoracic segments.

20 It also would be desirable to provide
inexpensive apparatus and methods for measuring cardiac
output using BIA techniques that overcome the drawbacks
of previously known BIA cardiac output measurement
devices and methods.

25 It would further be desirable to provide
apparatus and methods for continuously monitoring
cardiac output so as to permit the measured cardiac
output to be employed as a metric for controlling and
maintaining other aspects of a patient's health.

30 Summary Of The Invention

35 In view of the foregoing, it is an object of
this invention to provide apparatus and methods for
accurately, non-invasively and continuously measuring
cardiac output using BIA techniques.

It is another object of this invention to
provide apparatus and methods for measuring cardiac
output in critically ill patients using BIA techniques
that overcome the inaccuracies arising from measuring

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5 voltage changes across the whole body or large volume thoracic segments.

It is yet another object of the present invention to provide inexpensive apparatus and methods for measuring cardiac output using BIA techniques that
10 overcome the drawbacks of previously known BIA cardiac output measurement devices and methods.

It is still another object of this invention to provide apparatus and methods for continuously monitoring cardiac output that permit the measured
15 cardiac output to be employed as a metric for controlling and maintaining other aspects of a patient's health.

These and other objects of the invention are accomplished in accordance with the principles of the invention by providing BIA cardiac output monitoring
20 apparatus that can be disposed within a patient's airway (e.g., trachea and/or bronchus) in close relation to the ascending aorta to acquire cardiac output information. Apparatus in accordance with the present invention includes: 1) one or more sense
25 electrodes placed in the patient's trachea in the vicinity of the ascending aorta; 2) at least two current electrodes disposed either on an exterior surface of the patient's thorax or within the patient's trachea; and 3) optionally, at least one sense
30 electrode disposed on the patient's exterior surface in the vicinity of the suprasternal notch.

In accordance with the principles of the invention, current conducted between the current
35 electrodes flows throughout the thorax, and passes preferentially through blood because of its high conductivity, relative to other body materials. The sense electrodes primarily sense the voltage drop in the blood in the ascending aorta. Because the

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5 impedance of the blood in the aorta changes with the
volume of blood flowing through the aorta, the measured
voltage drop between the sense electrodes varies with
blood flow. The time-varying differences in the sensed
10 voltage, therefore, are primarily caused by blood flow
dynamics, rather than respiratory or non-cardiac
related physiological effects.

Methods in accordance with the present
invention overcome the inaccuracies of the gross
physiologic models employed in previously known BIA
15 cardiac methods, by avoiding the simplified algorithms
for the ventricular stroke volume based on whole thorax
BIA measurements. In particular, the methods of the
present invention avoid the inaccuracies in whole body
or thoracic BIA measurements associated with ignoring
20 the multiple, branched and complex paths of blood flow.

In accordance with the present invention, the
ability to obtain BIA measurements in the vicinity of
the ascending aorta, which has no branches other than
the coronary arteries, and which therefore closely
25 reflects the blood flow through the ascending aorta,
provides a simple and highly accurate metric for
computing ventricular stroke volume.

In yet further aspects of the present
invention, the apparatus for monitoring a patient's
30 cardiac output may be used to control administration of
intravenous fluids to a patient or to optimize heart
rate for those patients having pacemakers.

Brief Description Of The Drawings

35 Further features of the invention, its nature
and various advantages will be more apparent from the
accompanying drawings and the following detailed
description of the preferred embodiments:

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5 FIGS. 1A and 1B are idealized models of the volumes upon which previously known bioelectrical impedance algorithms are based;

 FIGS. 2A and 2B are a vertical frontal view of the upper portion of a human body and a front view
10 of the ascending aorta, the esophagus and the trachea, respectively;

 FIGS. 3A-3C are schematic views (including block diagrams) of members of a first family of embodiments of the present invention, wherein the
15 current electrodes are disposed on an external surface of the patient's thorax;

 FIGS. 4A-4C are schematic views (including block diagrams) of members of a second family of embodiments of the present invention, wherein the
20 current electrodes are disposed within the patient's airway;

 FIGS. 5A and 5B are, respectively, a perspective view and a cross-sectional view along view line 5B--5B, of an illustrative member of the first
25 family of embodiments of the present invention;

 FIGS. 6A and 6B are, respectively, a perspective view and a cross-sectional view along view line 6B--6B, of an illustrative member of the second family of embodiments of the present invention;

30 FIGS. 7A and 7B are, respectively, a perspective view and a cross-sectional view along view line 7B--7B, of an alternative member of the second family of embodiments of the present invention;

 FIG. 8 is a graph showing the relationship
35 between cardiac events and the first derivative of the bioelectrical impedance; and

 FIGS. 9A and 9B are, respectively, schematic diagrams showing systems for administering fluids to a patient and for controlling heart rate for patients

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5 having pacemakers, respectively, constructed in
accordance with the principles of the present
invention.

Detailed Description Of The Invention

10

The present invention relates generally to
BIA apparatus for use in measuring cardiac output in
patients, including critically ill and heart-diseased
patients, as well as patients undergoing elective
15 surgery. The apparatus and methods of the present
invention overcome drawbacks observed in previously
known attempts to use whole body or large volume
thoracic BIA measurements to measure cardiac output, by
providing apparatus and methods that are not based upon
20 the gross modeling of physiological events implicit in
such previously known BIA measurement techniques.

In a first family of embodiments of the
apparatus and methods of the present invention, two or
more sense electrodes are disposed in contact with a
25 patient's airway (trachea and/or bronchus) in close
relation to and along the axis of the ascending aorta,
so that changes in bioelectrical impedance can be
closely correlated to cardiac events, without
significant effects due to non-cardiac physiologic
30 events. Excitation AC current is injected into the
body between two or more current electrodes disposed on
the exterior of the patient's thorax. In a second
family of embodiments constructed in accordance with
the present invention, the excitation current is
35 injected into the patient's thorax by current
electrodes disposed in the patient's airway, preferably
in the vicinity of the pharynx and bronchus.

In both families of embodiments,
bioelectrical impedance is computed from the voltage
40 drop measured either between two or more of the sense

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5 electrodes disposed in the patient's airway or one or
more of the sense electrodes disposed in the patient's
airway and one or more external electrodes disposed in
the vicinity of the patient's suprasternal notch. The
value of bioelectrical impedance is in turn correlated
10 to blood flow through the ascending aorta. Because the
ascending aorta has no other branches other than the
coronary arteries, blood flow through the ascending
aorta may be closely correlated to cardiac output.

It is known in the medical literature that
15 BIA measurements of cardiac output in general show good
correlation for normal patients and hemodynamically
stable patients, but much poorer correlation for
critically ill patients, and patients in heart failure,
as discussed in the above-mentioned Detemeter paper.
20 Applicant has discovered that the reason for this
poorer correlation in the latter cases is that the
theoretical basis underlying the use of whole body or
large volume thoracic measurements may be incorrect.

While the present invention finds ready
25 application in monitoring cardiac output in critically-
ill and heart diseased patients, it may be
advantageously used for all intubated patients,
including pediatric cases. For example, apparatus
constructed in accordance with the present invention
30 may be readily employed in asymptomatic patients
undergoing elective surgery. As many as 95% of post-
operative deaths in the latter population result from
hemodynamic failure.

Previously known techniques derive the
35 equation for ventricular stroke volume ("SV") from the
assumption that a time-varying column of blood, in
parallel with the other conducting material in the
thorax, changes from zero to the full stroke volume
during the cardiac cycle. The column of blood is

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5 assumed to be the length between the electrodes used to obtain the BIA measurements, with effects on the BIA measurements due to respiration accounted for, for example, as discussed in the aforementioned U.S. Patent No. 4,870,578.

10 FIG. 1A illustrates a typical previously known BIA algorithm. Cardiac output is estimated from the bioelectrical impedance measurement $I(t)$, where it is assumed that changes in the bioelectrical impedance coincidental with the heart electrical activity (as
15 represented by an electrocardiograph output) are the result of blood flow $F(t)$. A transfer function $T(t)$ is then based upon empirical formulae derived from measurements taken on healthy, hemodynamically stable subjects. The bioelectrical impedance $I(t)$ is then
20 computed as:

$$I(t) = F(t) * T(t) \quad (1)$$

Applicant has determined, however, that the
25 foregoing assumption regarding the column of blood ignores the branched, multiple and complex paths present in the arterial system. Moreover, the distribution of blood and fluids between different physiologic "compartments" in the idealized thoracic or
30 whole body model and body regions are different in normal and critically ill patients.

FIG. 1B illustrates that the thoracic
approach to BIA measurement must account for transfer
functions appropriate to each of the multiple blood
35 flow paths through the volume, so that bioelectrical impedance $I(t)$ should be computed as:

$$I(t) = \sum F_i(t) * T_i(t) * W_i \quad (2)$$

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5 where W_i are weights corresponding to *a priori* knowledge
of the relative distribution of flow through the
various segments of the volume, e.g., the aorta, and
arterial segments and other fluid chambers. Moreover,
the weights W_i may be different for different patients,
10 may be different for chronically ill as opposed to
healthy subjects, and may be variable even within a
given patient, e.g., due to changes in heart rate.

Applicant has discovered, however, that
equation (1) may be used accurately for any patient
15 provided that the transfer function $T(t)$ is correlated
to measured blood flow (e.g., using a flow meter) so
that the effect of the distribution weights W_i can be
essentially eliminated. Accordingly, applicant has
concluded that BIA measurements should be taken very
20 close to a major blood vessel or artery, so that
between the electrodes of the BIA apparatus there are
few or no branching vessels or adjacent vessels. The
present invention therefore involves the use of BIA
measurements in the vicinity of blood vessels meeting
25 the foregoing requirements, especially the ascending
aorta.

Referring to FIG. 2A, the upper portion of a
human body 100 is shown in outline with the
corresponding locations of aorta 101, esophagus 102,
30 trachea 103, and bronchi 104a and 104b (all shown in
dotted line) and suprasternal notch 105. These
internal vessels and organs are more clearly depicted
in FIG. 2B. With reference to FIGS. 2A and 2B, the
outflow tract of the left ventricle of the heart is
35 ascending aorta 101a. Segment 101b of the artery (the
aortic arch) passes in front of right bronchus 104a, in
front of trachea 103 and then arches behind left
bronchus 104b into the descending aorta 101c, which
leads towards the lower part of the body.

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5 Applicant has observed that because ascending
aorta 101a passes in close proximity to bronchi 104a
and 104b and trachea 103, it is possible to obtain a
BIA measurement across ascending aorta 101a, with
relatively little intervening tissue, by positioning
10 two or more internal, or internal and external, sense
electrodes at this location. For example, a first
sense electrode may be disposed in trachea 103 and a
second sense electrode may be disposed on the patient's
external surface near suprasternal notch 105.
15 Alternatively, two or more sense electrodes may be
positioned within trachea 103 aligned with the axis of
ascending aorta 101a, so that at least a first sense
electrode is disposed above aortic arch 101b and a
second sense electrode is disposed at a level just
20 below aortic arch 101b.

AC voltage applied to the patient's tissue by
current electrodes, positioned either on the external
surface of the patient or within the patient's airway,
causes an AC current to flow in the patient's tissue.
25 The measured voltage difference between the sense
electrodes is then employed to compute tissue
impedance. Because the first branches from the aorta
(other than the coronary arteries) are from aortic arch
101b, downstream of the measurement location, the
30 measurement of blood flow from ascending aorta 101a
accurately measures the volume of blood ejected from
the left ventricle.

Moreover, the calculated bioelectrical
impedance $I(t)$ in equation (1) comprises both a desired
35 signal $S(t) = F(t) \cdot T(t)$, due to aortic blood flow, and
a noise component, $N(t)$, caused by non-cardiac related
physiological effects, such as body motion and
respiratory effects. The signal-to-noise ratio ("SNR")
is computed as:

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$$5 \quad \text{SNR} = S(t)/N(t) \quad (3)$$

Accurate measurement of cardiac output requires averaging repeated BIA measurements. If the SNR can be increased, however, less averaging is required to achieve accurate blood flow measurements. Applicant has observed that the SNR is affected by the position of the sense electrodes, and more particularly, that improved SNR may be attained by providing the sense electrodes with preferred orientations relative to the ascending aorta, as described in greater detail hereinbelow.

Apparatus of the present invention is described with respect to two families of embodiments. In the first family of embodiments, excitation AC current is applied to the patient's thorax by two or more current electrodes disposed on an external surface of the thorax; in a second family of embodiments, the current electrodes are disposed within the patient's airway. It is contemplated that the choice of placement of the current electrodes will not substantially effect the BIA values or corresponding cardiac output measurements. Rather, the choice of using internal versus external current electrodes relates to the particular use of the apparatus. For example, internal electrodes may be desirable to reduce the number of wires crossing a sterile operating field, while external electrodes may be desirable for certain short-term cardiac output monitoring situations.

Referring now to FIGS. 3A-3C, illustrative members of a first family of embodiments of the present invention are described. In FIG. 3A, apparatus 10 constructed in accordance with the principles of the present invention is described. Apparatus 10 includes sense electrode apparatus 11, external sense electrode

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5 12, current electrodes 13, impedance recorder 110, digital sampler 112 and computer 114. In FIGS. 3, the patient's thorax is denoted by reference numeral 100 while the aortic arch is indicated in cross-section by reference numeral 106.

10 Sense electrode apparatus 11 comprises endotracheal tube 17 having inflatable cuff 18, a lumen for ventilating the patient, and at least one, and preferably two or more, sense electrodes 19. Sense electrodes 19 are carried on wires 20 slidably disposed
15 in lumens of the endotracheal tube (as shown, for example, in FIG. 5B). Wires 20 deflect outwardly when moved to their deployed position, to urge sense electrodes 19 into contact with the interior surface of the trachea and/or the bronchi.

20 External sense electrode 12 is preferably disposed on the surface of the patient's thorax, in or near the suprasternal notch, while current electrodes 13 are disposed on an exterior surface of patient's thorax 100 at positions adequate to bracket the sense
25 electrodes. External sense electrode 12 may comprise a spot EKG electrode, for example, model AMI 1750-001, manufactured by Medtronic-Andover Medical, Boston, Massachusetts. Sense electrode apparatus 11, external sense electrode 12, and current electrodes 13 are
30 coupled to impedance recorder 110 by electrical leads 21. Inflatable cuff 18 engages the interior wall of the trachea to retain and stabilize endotracheal tube 17 in position.

35 Impedance recorder 110 may be a commercially available impedance recorder providing both the current injected by current electrodes 13 (generally less than 1 mA at a frequency of 50-100 kHz) and impedance measuring capability, for example, the Minnesota Impedance Cardiograph Model 304A, operating at 100 kHz.

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5 Signals output from the impedance recorder are
digitally sampled by digital sampler 112, for example,
at a rate of 250 Hz using a standard 12-bit analog to
digital converter, available from ComputerBoards, Inc.,
Mansfield, Massachusetts. The sampled output of
10 digital sampler 112 is then provided to computer 114,
for example, an IBM-compatible personal computer having
an Intel 386 or higher microprocessor, for storage and
processing, as described hereinafter.

BIA measurements are obtained by injecting
15 current through current electrodes 13 and measuring the
voltage between a selected one of the sense electrodes
19 on sense electrode apparatus 11 and external sense
electrode 12. In this manner, the voltage drop sensed
by apparatus 10 corresponds primarily to that induced
20 by blood flow changes through the ascending aorta. By
providing two or more sense electrodes on endotracheal
tube 17, sense electrode 19 closest to aortic arch 106
may be selected for use in combination with external
sense electrode 12 to measure the voltages used in
25 determining bioelectrical impedance. Thus, for
example, the clinician may use combinations of external
electrode 12 in combination with each of sense
electrodes 19 in sequence, to determine which provides
the strongest signal, and hence, the best measure of
30 cardiac output.

Alternatively, the voltage drop between sense
electrodes 19 may be used directly to compute
bioelectrical impedance, without the use of external
sense electrode 13. In this instance, endotracheal
35 tube 17 is positioned within the trachea (using for
example, radiographic markers disposed on the tube) so
that one of sense electrodes 19 is located at a height
even with, or slightly above, aortic arch 106, while
another sense electrode 19 is disposed at a height just

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5 below the aortic arch. When two or more sense electrodes are provided on sense electrode apparatus, the clinician may evaluate various combinations of the sense electrodes to determine which provides the strongest signal.

10 Referring now to FIG. 3B, apparatus 30 is described. Apparatus 30 is similar to that of FIG. 3A, such as described in the preceding paragraph, and comprises sense electrode apparatus 31, current electrodes 32, impedance recorder 110, digital sampler
15 112 and computer 114. Sense electrode apparatus includes endotracheal tube 33 having inflatable cuff 34 and at least proximal and distal sense electrodes 35 and 36. In this embodiment, proximal and distal sense electrodes are arranged so that, when fully deployed, a
20 line connecting the two electrodes forms an angle α with respect to the longitudinal axis of the endotracheal tube.

One of current electrodes 32 is applied to thorax 100 proximally of proximal sense electrode 35
25 while the other current electrode is applied to the thorax distally of distal electrode 36, so that the current electrodes bracket the sense electrodes. Current from impedance recorder 110 is injected into the patient's thorax 100 by current electrodes 32, and
30 sensed by proximal and distal sense electrodes 35 and 36. The voltage drop between sense electrodes 35 and 36 is then employed to determine impedance.

In accordance with one aspect of the present invention, the angle α formed between sense electrodes
35 35 and 36 and the longitudinal axis of the endotracheal tube is preferably in a range of between 25 and 45 degrees. Applicant has determined that orientation of the sense electrodes in this manner will account for angulation in the aortic anatomy. In particular,

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5 applicant expects that by positioning the proximal and distal sense electrodes at an angle with respect to endotracheal tube 31, the sense electrodes will be more nearly aligned with the axis of the ascending aorta, as opposed to the embodiment of FIG. 3A.

10 Referring now to FIG. 3C, apparatus 40 is described. Apparatus 40 constitutes a modified form of apparatus 30 of FIG. 3B, and comprises sense electrode apparatus 41, current electrodes 42, impedance recorder 110, digital sampler 112 and computer 114. Sense
15 electrode apparatus 41 includes endotracheal tube 43 having inflatable cuff 44, proximal sense electrodes 45 and 46 and distal sense electrodes 47 and 48. Proximal sense electrode 46 and distal sense electrode 47 are arranged so that, when fully deployed, a line
20 (accounting for the curvature of the endotracheal tube) connecting the two electrodes forms an angle α with respect to the longitudinal axis of the endotracheal tube. Proximal sense electrode 45 and distal sense electrode 48 are also arranged so that, when fully
25 deployed, a line connecting the two electrodes forms an angle β with respect to the longitudinal axis of the endotracheal tube. Current electrodes 42 are disposed on thorax 100 so as to bracket all of the sense electrodes on sense electrode
30 apparatus 41.

 The angle α formed between sense electrodes 46 and 47 and the longitudinal axis of the endotracheal tube is preferably in a range of between 25 and 45 degrees, while angle β correspondingly is in a range of
35 65 to 45 degrees. Preferably, sense electrodes 45 and 48 are orthogonal to electrode pair 46 and 47. Thus, whereas sense electrodes 46 and 47 will be more nearly aligned with the axis of the ascending aorta ("on-

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5 axis"), sense electrode pair 45 and 48 will be oriented normal to the axis of the aorta ("normal-to-axis") and provide a signal effected by non-blood flow effects, such as respiratory effects and cardiac wall motion.

Accordingly, the voltage drop measured
10 between sense electrodes 46 and 47 may be used to calculate an "on-axis" impedance, corresponding to blood flow through the ascending aorta and any non-cardiac effects, while the voltage drop measured between sense electrodes 45 and 48 may be used to
15 calculate a "normal-to-axis" impedance that is expected to correspond primarily to non-blood flow effects. Applicant contemplates that by subtracting the normal-to-axis impedance from the on-axis impedance, the resulting impedance value will correspond predominantly
20 to blood flow, and have a higher SNR than may be attained with the apparatus of FIGS. 3A or 3B.

Referring now to FIGS. 4A-4C, the second family of embodiments of the present invention are described. In the following descriptions of FIGS. 4A-
25 4C, impedance recorder 110, digital sampler 112, and computer 114 provide the same functionality as described hereinabove with respect to FIGS. 3, and will therefore be omitted from further detailed discussion.

With respect to FIG. 4A, a first illustrative
30 member of the second family of embodiments of the present invention is described. Apparatus 50 is similar to that described above with respect to FIG. 3A, except that in apparatus 50 the current electrodes are disposed on the endotracheal tube, rather than the
35 exterior surface of the thorax. In particular, apparatus 50 includes endotracheal tube 51, two or more sense electrodes 52, external sense electrode 53, inflatable cuffs 53 and 54, and proximal and distal current electrodes 55 and 56 mounted on inflatable

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5 cuffs 53 and 54, respectively. Electrodes 52, 53, 55 and 56 are coupled to impedance recorder 110 by leads 57.

Proximal current electrode 55 is disposed in the patient's trachea so that it contacts either the
10 pharynx or larynx when inflatable cuff 55 is inflated. Distal current electrode 56 is disposed to contact the interior wall of the patient's trachea, for example, at a height below the xiphoid process, when inflatable cuff 54 is inflated. Current electrodes 55 and 56
15 conduct an AC excitation current from impedance recorder 110 to the patient's thorax.

Sense electrodes 52 and 53 may be employed as described hereinabove with respect to FIG. 3A. In particular, impedance values may be determined based
20 upon either voltages measured between a selected one of sense electrodes 52 and external electrode 53, between sense electrodes 52 positioned above and below aortic arch 106, or a combination thereof.

In FIG. 4B, an alternative member of the
25 second family of embodiments is described. Apparatus 60 mirrors apparatus 30 of FIG. 3B, except that apparatus 60 includes proximal and distal current electrodes 67 and 68 disposed on inflatable cuffs 64 and 65 respectively. Proximal and distal sense
30 electrodes 62 and 63 are arranged so that, when fully deployed, a line between the two electrodes forms an angle α with respect to the longitudinal axis of endotracheal tube 61. Angle α preferably is in a range of between 25 to 45 degrees, so that the electrodes are
35 more nearly aligned with the axis of the ascending aorta.

In FIG. 4C, a further alternative member of the second family of embodiments is described. Apparatus 70 is similar to that described above with

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5 respect to apparatus 40 of FIG. 3C. Apparatus 70
includes proximal and distal current electrodes as
described with respect to FIG. 4B, and which operate in
like manner to serve a like purpose. Apparatus 70
includes a pair of "on-axis" sense electrodes 72 and 73
10 and a pair of "normal-to-axis" electrodes 74 and 75, as
described above with respect to FIG. 3C. Applicant
expects that apparatus 70 will provide higher SNR than
the embodiments of FIGS. 4A and 4B, because respiratory
effects and wall motion artifacts may be removed from
15 the impedances by taking differences between the "on-
axis" voltage drop and the "normal-to-axis" voltage
drop.

Referring now to FIGS. 5A and 5B, an
illustrative embodiment of sense electrode apparatus 80
20 similar to that of FIG. 3B is described in greater
detail. Apparatus 80 comprises endotracheal tube 81
carrying proximal sense electrode 82, distal sense
electrode 83, and inflatable cuff 84. As shown in FIG.
5B, endotracheal tube 81 includes lumen 85 for
25 providing ventilation to the patient during intubation,
lumen 86 through which proximal sense electrode 82 may
be reciprocated, lumen 87 through which distal sense
electrode 83 may be reciprocated, and lumen 88 for
inflating inflatable cuff 84.

30 Sense electrodes 82 and 83 preferably
comprise electrically insulated stainless steel wires
about 0.020 inches (0.051 mm) thick that are pre-
stressed to deflect outwardly when extended from lumens
86 and 87, thus urging the electrodes into contact with
35 the interior wall of the patient's airway (e.g.,
trachea or bronchus). Each of sense electrodes 82 and
83 preferably includes an exposed ellipsoidal or
spherical region at its distal end that provides an
atraumatic tip. Sense electrodes are arranged so that,

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5 when fully deployed from lumens 86 and 87, a line
between the tips of the electrodes preferably forms an
angle in a range of between 25 and 45 degrees with
respect to the longitudinal axis of the endotracheal
tube.

10 Sense electrode 82 enters lumen 86 through
opening 90 at the proximal end of endotracheal tube 81
and exits lumen 86 through skive 91 that opens to the
lateral face of endotracheal tube 81. Sense electrode
83 enters lumen 87 through opening 92 and exits lumen
15 87 through skive 93 near the distal end of endotracheal
tube 81. Each of the sense electrodes preferably
includes a 0.0005 inch (0.013 mm) thick layer of
insulation over the length of the electrode that
extends outside of lumens 86 and 87, respectively,
20 except that the ellipsoidal or spherical members at the
distal ends of the electrodes are uninsulated to
provide electrical connection to the interior wall of
the patient's airway.

Each of sense electrodes 82 and 83 includes a
25 proximal end having positioning and locking hub 94, and
is disposed for sliding movement through connector
block 95. Connector block 95 permits a sliding
electrical connection to be established between each
sense electrode and the connector block, while
30 permitting the sense electrodes to be moved proximally
and distally therethrough. Plug 96 couples sense
electrodes 82 and 83 to impedance recorder 110 via
cable 97 electrically connected to connector block 95.

The interior of inflatable cuff 84 is in
35 fluid communication with insufflation port 98 via lumen
88 of endotracheal tube 81. When inflated, inflatable
cuff 84 retains endotracheal tube 81 in position within
the patient's airway, thereby preventing inadvertent
movement of the endotracheal tube. Inflatable cuff 84

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5 also assists in urging sense electrodes 82 and 83 into
contact with the interior wall of the trachea.
Inflatable cuff 84 may be inflated using conventional
inflation means (i.e., a liquid filled syringe or
pressurized gas cylinder) connected to insufflation
10 port 98 via lumen 88. Alternatively, inflatable cuff
84 may be replaced by another suitable type of
expandable member for urging the sense electrodes
against the interior wall of the patient's airway, such
as an expanding mandrel, or other mechanical
15 arrangement.

The proximal end of endotracheal tube 81,
i.e., the end manipulated by the clinician, may include
reference marks 99 on the circumference of the tube
that reflect the circumferential orientation of
20 electrodes 82 and 83 within the patient's trachea. The
reference marks may be used to ensure proper
registration of electrodes 82 and 83 with the portion
of the tracheal wall nearest to the ascending aorta.

In an alternative embodiment of sense
25 electrode apparatus of FIGS. 5 (not shown), more than
two sense electrodes may be disposed on the
endotracheal tube, so that the signals received from
the electrodes may be optimally configured by the
clinician after the endotracheal tube has been disposed
30 in the patient's trachea. In this manner, a certain
pair of the sense electrodes may be selected to provide
an optimal output according to some predetermined
metric, for example, the highest SNR. In such an
embodiment, the impedance recorder or digital sampler
35 may be modified to include suitable selection and
switching logic, either as hardware or software, to
select which sense electrodes contribute to the
computed cardiac output.

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5 Referring now to FIGS. 6A and 6B, an illustrative embodiment of apparatus 120 similar to that of apparatus 70 of FIG. 4C is described in greater detail. Apparatus 120 comprises endotracheal tube 121 carrying proximal sense electrodes 122 and 123, distal
10 sense electrodes 124 and 125, and current electrodes 126 and 127 disposed on inflatable cuffs 128 and 129. As shown in FIG. 6B, endotracheal tube 121 includes lumen 130 for providing ventilation to the patient during intubation, lumens 131 and 132 through which
15 proximal sense electrodes 122 and 123 may be reciprocated, lumens 133 and 134 through which distal sense electrodes 124 and 125 may be reciprocated, lumen 135 through which the electrical leads wires 136 for current electrodes 126 and 127 extend, and lumens 137
20 and 138 for inflating inflatable cuffs 128 and 129, respectively.

Sense electrodes are arranged so that, when fully deployed from their respective lumens, a line between the tips of electrodes 123 and 125 preferably
25 forms an angle in a range of between 25 and 45 degrees with respect to the longitudinal axis of the endotracheal tube, thus approximating the angular orientation of the aortic anatomy. Also, a line between sense electrodes 122 and 124, when those
30 electrodes are fully deployed, preferably is orthogonal to a line between electrodes 123 and 125. Apparatus 120 thereby permits determination of impedances "on-axis" and "normal-to-axis" as described with hereinabove with respect to FIG. 4C.

35 Sense electrodes 122-125 enter respective lumens 131-134 through openings near the proximal end of endotracheal tube 121, exit the respective lumens through skives that open to the lateral face of the endotracheal tube, and are reciprocable through the

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5 lumens in the same manner as sense electrodes 82 and 83
of the embodiment of FIGS. 5. Sense electrodes
likewise are constructed as described above with
respect to the embodiment of FIGS. 5, and are
electrically coupled to plug 139 via connector block
10 140 and cable 141.

Inflatable cuffs 128 and 129 are in fluid
communication with insufflation ports 142 via lumens
137 and 138 of endotracheal tube 121, and may be
inflated as described above with respect to the
15 embodiment of FIGS. 5. When inflated, inflatable cuffs
128 and 129 retain endotracheal tube 121 in position
within the patient's airway, and serve to urge current
electrodes 126 and 127 into electrical contact with the
interior wall of the patient's airway.

20 Current electrodes 126 and 127 preferably
comprise conductive foil strips about 6 to 10 cm in
height, for example, Type M6001, available from the 3M
Company, St. Paul, Minnesota, and may extend around the
entire circumferences of inflatable cuffs 128 and 129,
25 or may extend over only a portion of the circumference.
The current electrodes may be disposed on the exterior
of the inflatable cuffs using a suitable adhesive or
fastening means. Proximal current electrode 126 is
preferably connected to electrical ground.
30 Alternatively, if inflatable cuffs 128 and 129 are
eccentrically shaped, the current electrodes may be
attached directly to the exterior of endotracheal
tube 121.

The proximal end of endotracheal tube 121 may
35 also include reference marks to assist in determining
the circumferential orientation of the endotracheal
tube within the patient's airway.

An alternative embodiment of the apparatus of
FIGS. 6 is now described with respect to apparatus 150

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5 of FIGS. 7A and 7B. Apparatus 150 comprises
endotracheal tube 151 having proximal spot-type sense
electrodes 152 and 153, and distal spot-type sense
electrodes 154 and 155, disposed on elongate inflatable
member 156, and current electrodes 157 and 158
10 disposed, respectively, on inflatable cuffs 159 and
160. In accordance with the high SNR aspect of the
invention, a line between electrodes 153 and 154
preferably forms an angle α in a range of between 25
and 45 degrees with respect to the longitudinal axis of
15 endotracheal tube 151, and orthogonal to a line between
electrodes 152 and 155.

Elongate inflatable member 156 is
inflated by insufflation port 161 via lumen 162 (see
FIG. 7B), while inflatable cuffs 159 and 160 are
20 inflated via insufflation port 163 and lumen 164, and
insufflation port 165 and lumen 166, respectively.
Electrical lead wires coupling current electrodes 158
and 159 to plug 167 are routed through lumen 168, while
electrical lead wires coupling sense electrodes 152-155
25 to plug 169 are routed through lumen 170. Endotracheal
tube 151 includes passageway 171 for providing
ventilation and administering oxygen during intubation.
The proximal end of endotracheal tube 121 may also
include reference marks for determining the
30 circumferential orientation of the endotracheal tube
when inserted in the patient's airway.

When inflated, elongate inflatable member
156, which may be eccentric in shape, urges sense
electrodes 152-155 into electrical contact with the
35 interior of the patient's airway. Likewise, inflatable
cuffs 159 and 160 urge current electrodes into
electrical contact with the interior walls of the
patient's airway at locations proximal and distal to
elongate inflatable member 156.

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5 Current electrodes 158 and 159 may comprise
conductive foil strips of the type mentioned
hereinabove, and may extend around the entire
circumferences of inflatable cuffs 128 and 129, or may
extend over only a portion of the circumference. Sense
10 electrodes 152-155 may likewise be fashioned from
conductive foil strips or from spot-type EKG
electrodes, also as described hereinabove. The current
and sense electrodes are fastened to the exterior of
the inflatable member and cuffs using a suitable
15 adhesive or fastening means.

Operation of any of the above-described
embodiments of the present invention is now briefly
described. First, the endotracheal tube is inserted
into the patient through the nasal cavity, past the
20 epiglottis and into the trachea in accordance with
standard intubation practice. If the apparatus of the
present invention is to be used for only a relatively
short period of time, e.g., while a patient is
anesthetized during surgery, an endotracheal tube
25 alternatively may be inserted into the trachea via the
mouth. Alternatively, access to the trachea may be had
through a surgical opening at the suprasternal notch by
conventional tracheotomy.

Using the reference marks on the
30 circumference of the proximal end of the endotracheal
tube (if present), the clinician may manipulate the
endotracheal tube to ensure proper orientation of the
endotracheal tube within the patient's airway. The
inflatable cuff or cuffs then are inflated to stabilize
35 the endotracheal tube, and the hubs of the sense
electrodes are moved distally to deploy the sense
electrodes into electrical contact with the interior
wall of the patient's trachea and/or bronchus (or for
the embodiment of FIGS. 7, the elongate inflatable

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5 member is inflated). The current electrodes are either urged into contact with the interior of the patient's airway, by inflating the inflatable cuffs, or are separately applied to the external surface of the patient. The sense electrodes (optionally including
10 the external sense electrode) and current electrodes are then connected to impedance recorder 110. Bioelectrical impedance values may be then determined for processing as described hereinbelow.

A method of computing cardiac output in
15 accordance with the well-known Kubicek equation is now described. Referring to FIG. 8, the first derivative of the measured impedance (dZ/dt) (curve I) is compared to a typical electrocardiograph waveform (curve II) for a normal patient, where the components of the waveform
20 describing events within the cardiac cycle are labeled. Curve I includes an A-wave component, due to atrial activity at the beginning of the cardiac cycle, represented by a downward deflection in the curve. The I-wave component represents an upward deflection in
25 curve I occurring during isometric contraction. The B-wave component corresponds to the start of blood flow out of the ventricles, while the C-wave component of curve I represents the major upward deflection during the cardiac cycle. The amplitude of this deflection,
30 measured from the zero point, is used in the calculation of the ventricular stroke volume ("SV"). The X and Y points of curve I reflect closure of the aorta and pulmonary valves, respectively. Point O corresponds to rapid filling of the ventricles.

35 SV is calculated according to equation (4) as:

$$SV = \rho(L/Z_0)^2 * (dZ/dt_p) \tau \quad (4)$$

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5 where:

- SV = ventricular stroke volume, ml;
ρ = resistivity of blood (in normal
 patients, about 150-200 ohm-cm/s, and
 can be corrected for each patient as a
10 function of hematocrit);
L = distance between the sense electrodes,
 cm;
Z₀ = mean impedance between the measurement
 electrodes, ohms;
15 dZ/dt_p = peak value of the upward deflection in
 the first derivative of the impedance
 waveform (amplitude of C-wave); and
τ = ventricular ejection time (computed as
 the period between the occurrence of the
20 B-wave component and point X in curve
 I).

 The digitized first derivative of the
impedance determined by the impedance recorder is
analyzed to extract the B-wave and C-wave components
25 and the X deflection point. The amplitude of the B-C-X
portion of the curve I waveform, and the time between
these segments are then employed to compute stroke
volume using equation (4). The distance between the
electrodes L is either known as a manufacturing
30 parameter (where the sense electrodes are all on the
endotracheal tube) or may be computed based on external
dimensions (where an external sense electrode is
employed, as in FIG. 3A).

 In a preferred embodiment of the invention,
35 SV is continuously computed for each data segment that
is of good signal quality, i.e., where the amplitude of
the derivative of the impedance signal is above a
certain quality metric. The SV may be continuously
updated on a display (not shown) associated with

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5 computer 114, and may consist of a running average of the current and a user-selectable number of preceding cardiac cycles. Cardiac output may then be computed as the product of the instantaneous average SV and the heart rate, and also displayed numerically.

10 Alternatively and in accordance with the methods of the present invention, equations for computing cardiac output using the apparatus of the present invention may be derived as follows:

15 The cross-sectional area, a , of a cylindrical vessel may be computed as:

$$a = (1/Z - 1/Z_0) \rho L = (\Delta Z / Z Z_0) \rho L \approx \Delta Z \rho L / Z^2_0 \quad (5)$$

20 where Z is the measured electrical impedance; Z_0 is the baseline electrical impedance; ρ is the resistivity of blood (typically 150-200 ohm-cm); L is the spacing between the sense electrodes; and $\Delta Z = Z - Z_0$.

25 The instantaneous flow of blood, Q , through blood vessels of cross-sectional area a may be computed from:

$$Q = a^2 P / 8 \eta L \eta \quad (6)$$

30 where η is the dynamic viscosity of blood, P is the average blood pressure drop along the blood vessel (a linear function of the maximum difference during the cardiac cycle) and L is the inter-electrode spacing.

35 Cardiac Output ("CO") therefore may be computed by integrating Q over predefined intervals (e.g., one minute intervals):

$$CO = \int Q \, dt \quad (7)$$

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5 Applicant has observed that even in the
simple parallel cylindrical model referred to in FIG.
1B, the relation between impedance changes and cardiac
output is complex and dependent on the electrode
configuration as well as multiple time-varying
10 physiological parameters. Known bio-impedance
algorithms, such as the Kubicek equation (equation
(4)), when used with previously known apparatus, do not
account for this complexity, and therefore have
achieved limited clinical use.

15 In accordance with the present invention,
however, the sense electrodes may be disposed in close
proximity to the ascending aorta, which initial testing
has shown to provide a sharp and reproducible waveform
that linearly tracks the ascending aorta blood flow
20 waveform (as determined by an implanted flow meter).
This linear time-varying (i.e., with cardiac cycle)
relationship between blood flow and impedance change
may be described as:

$$25 \qquad Q(t) = T(G, Z_0, t) \Delta Z(t) \qquad (8)$$

where Q is the computed blood flow; T is a transfer
function; G is a constant dependent upon the inter-
electrode spacing and size of the electrodes; and t is
30 the time interval relative to the cardiac cycle (e.g.,
the p wave of the EKG).

The transfer function T of equation (8) is
empirically derived from in-vivo experiments in
patients with in-dwelling flow probes and continuous
35 impedance measurements. A look-up table, $LUT(t)$, is
generated from the above-described experiments and is
used to estimate the instantaneous flow Q . CO is then
calculated based on the integral of Q over, for
example, a one minute period, or by integrating the

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5 ensemble average of one cardiac cycle and multiplying by the heart rate:

$$CO \approx K/Z^2_0 \int LUT(t) \Delta Z(t) dt \quad (9)$$

10 where K is an empirically-derived constant.

Further alternative embodiments of the present invention also may include additional sensors to enable other types of quantitative analysis. For example, diodes suitable for employing blood oximetry techniques based on near infrared light absorption also
15 may be disposed on the endotracheal tube to measure blood oxygen saturation levels. In particular, multiple light emitting diodes, including one or more red-light and infrared emitting diodes, may be disposed
20 on the endotracheal tube, on the inflatable cuff or member, or both, for obtaining blood oxygen saturation measurements using transreflectance oximetry techniques, as described, for example, in U.S. Patent 5,099,842, the entirety of which is incorporated herein
25 by reference.

Referring now to FIG. 9A, use of the apparatus of the present invention is described as a controller for fluids administration. In FIG. 9A, cardiac output is measured by apparatus 170, which may
30 be any of the foregoing embodiments, and includes endotracheal tube 171 disposed in patient 200. Apparatus 170 is used to monitor hemodynamic status and as a metric to control the administration of fluids intravenously via lumen 172 coupled to fluid supply
35 system 173. Computer 174, which may be an IBM-compatible PC (and, for example, the same computer that computes cardiac output from the impedance values output by impedance recorder 110 and digital sampler 112), controls fluid supply system 172.

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5 Operation of the apparatus of FIG. 9A is as follows. After a one unit loss of blood, for example, it is known that cardiac output changes but that heart rate and blood pressure do not. Thus, decreased cardiac output can be used to monitor the amount of
10 fluids to be given to a patient. The apparatus of FIG. 9A provides a closed-loop system wherein the amount of fluid injected into the patient is controlled by the cardiac output computed as described hereinabove. In particular, a baseline cardiac output measurement is
15 obtained and then a bolus of 50 cc of fluid is given while cardiac output is measured continuously. As long as the cardiac output increases, additional boluses of fluid are given periodically, e.g., every 15 minutes. This process may be repeated several times a day for a
20 critically ill patient.

 Referring now to FIG. 9B, use of the apparatus of the present is described as a controller for pacemaker 180. Generally, it is desirable to maximize cardiac output for the lowest possible heart
25 rate, since the lower the heart rate, the lower the myocardial oxygen consumption. In the arrangement of FIG. 9B, cardiac output is measured by apparatus 181, which may be any of the foregoing embodiments, and includes endotracheal tube 182 disposed in patient 200.
30 The output of apparatus 181 is used, in conjunction with computer 183, as a metric to control the setting of pacemaker 180 as described hereinafter.

 A baseline cardiac output measurement is first obtained and then the heart rate is reduced by a
35 predetermined amount, e.g., two beats/min, while the cardiac output is continuously monitored by apparatus 181. As long as the cardiac output increases or remains unchanged, the heart rate is periodically further lowered by the predetermined amount, for

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5 example, by 2 beats/min every 15 minutes. The process
of reducing heart rate while monitoring cardiac output
is continued until either a minimum desired heart rate
is obtained or the cardiac output measured by apparatus
181 begins to decrease. If the cardiac output is
10 determined to have decreased, the heart rate is
returned to the preceding higher rate.

Initial testing of the methods and apparatus
constructed in accordance with the present invention
has yielded results comparable to catheterization
15 techniques, but with a continuous output. Animal tests
have been conducted using an implanted occluder within
the inferior vena cava to vary preload and a Doppler
ultrasound flow probe implanted on the ascending aorta
to obtain samples for correlation to the output of the
20 bio-impedance recorder. Good correlation of the
Doppler measurements to the bio-impedance determined
with apparatus similar to that of FIG. 4A has been
obtained. In addition, no damage to tracheal mucosa
has been observed, even after extended periods of
25 intubation.

Although preferred illustrative embodiments
of the invention are described above, it will be
obvious to one skilled in the art that various changes
and modifications may be made therein without departing
30 from the invention and that the appended claims are
intended to cover all such changes and modifications
which fall within the true spirit and scope of the
invention. For example, applicant expects that the
apparatus and methods of the present invention may be
35 advantageously applied to animal subjects employed in
clinical studies, as well as humans.

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What Is Claimed Is:

1. Apparatus for use in combination with a bioelectrical impedance recorder and circuitry for processing the output of the bioelectrical impedance recorder to compute a metric corresponding to a patient's cardiac output, the apparatus comprising:

an endotracheal tube having a proximal portion, a distal portion, and a longitudinal axis;
first and second sense electrodes disposed on the distal portion and electrically coupled to the bioelectrical impedance recorder, the first and second sense electrodes spaced apart a first distance along the longitudinal axis;

means for urging the first and second electrodes against an interior wall of the patient's airway;

first and second current electrodes electrically coupled to the bioelectrical impedance recorder for injecting a sense current into the patient's thorax, the first and second current electrodes spaced apart a second distance greater than the first distance,

wherein the first and second sense electrodes generate a signal corresponding to the bioelectrical impedance of blood flow through the aorta and the signal is provided to the bioelectrical impedance recorder.

2. The apparatus as defined in claim 1 further comprising an external sense electrode coupled to the bioelectrical impedance recorder, one of the first and second sense electrodes and the external sense electrode generating an alternate signal corresponding to the bioelectrical impedance of blood

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flow through the aorta, the alternate signal being provided to the bioelectrical impedance recorder.

3. The apparatus as defined in claim 1 wherein the current electrodes are disposed on the endotracheal tube.

4. The apparatus as defined in claim 1 wherein the second sense electrode is located circumferentially away from the first sense electrode, so that a line intersecting the first and second sense electrodes forms an angle α relative to the longitudinal axis of the endotracheal tube.

5. The apparatus as defined in claim 4 wherein the angle α is a range of 25 to 45 degrees.

6. The apparatus as defined in claim 4 further comprising third and fourth sense electrodes disposed on the endotracheal tube, the third sense electrode disposed near, but circumferentially spaced apart from, the first sense electrode and the fourth sense electrode disposed near, but circumferentially spaced apart from, the second sense electrode, so that a line intersecting the third and fourth sense electrodes is orthogonal to a line intersecting the first and second sense electrodes.

7. The apparatus as defined in claim 1 wherein the endotracheal tube comprises at least first and second lumens, the first and second sense electrodes comprising first and second wires disposed for sliding movement through the first and second lumens, respectively.

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8. The apparatus as defined in claim 7 wherein the first and second wires include pre-stressed portions that cause the first and second sense electrodes to deflect outwardly when extended from the first and second lumens, respectively, the pre-stressed portions constituting the means for urging.

9. The apparatus as defined in claim 1 wherein the endotracheal tube further comprises an expandable member for retaining the endotracheal tube at a desired location in the passageway.

10. The apparatus as defined in claim 9 wherein the expandable member constitutes the means for urging.

11. The apparatus as defined in claim 10 wherein the endotracheal tube includes an expandable member and the first and second sense electrodes are disposed upon the expandable member.

12. The apparatus as defined in claim 9 wherein the expandable member is an inflatable cuff, and the endotracheal tube further comprises a lumen for inflating the inflatable cuff.

13. The apparatus as defined in claim 1 wherein at least one of the current electrodes is disposed on an inflatable cuff.

14. The apparatus as defined in claim 1 wherein the endotracheal tube is adapted to be inserted in the trachea of the patient through the mouth, a nasal passageway, or a tracheotomy port.

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15. The apparatus as defined in claim 1 wherein the apparatus further comprises reference marks on the proximal end of the tube to determine circumferential orientation of the endotracheal tube within the patient's trachea.

16. The apparatus as defined in claim 1 further comprising a fluid administration system for injecting a bolus of fluid into the vascular system of the patient, the fluid administration system coupled to the circuitry for processing and responsive to the metric corresponding to the cardiac output.

17. The apparatus as defined in claim 1 further comprising a pacemaker controlling the heart rate of the patient, the pacemaker coupled to the circuitry for processing and responsive to the metric corresponding to the cardiac output.

18. A method of measuring the cardiac output of an organism comprising steps of:

positioning first and second sense electrodes within an airway of the organism in the vicinity of the ascending aorta, the first and second electrodes spaced apart a first distance;

coupling first and second current electrodes to inject a current into the thorax of the organism, the first and second current electrodes spaced apart a second distance greater than the first distance;

applying a voltage between the first and second current electrodes so that a current flows through the tissues of the organism disposed along the second distance between the first and second current electrodes; and

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detecting a voltage developed across the first and second sense electrodes caused by the current flowing in the tissues of the organism, the voltage varying in accordance with changes in the bioelectrical impedance of the tissues.

19. The method as defined in claim 18 wherein the step of positioning the first and second sense electrodes in an airway of the organism further comprises steps of:

positioning the first sense electrode within the trachea of the organism near the ascending aorta; and

positioning the second sense electrode within the trachea of the organism so that the first and second electrodes are aligned with an axis of the ascending aorta of the organism.

20. The method as defined in claim 18 wherein the step of positioning the first and second current electrodes comprises a step of positioning the first and second current electrodes on an external surface of the organism.

21. The method as defined in claim 18 wherein the first and second sense electrodes are disposed on an endotracheal tube and the step of positioning the first and second sense electrodes further comprises a step of inserting the endotracheal tube in the trachea of the organism through a nasal passageway, the mouth of the organism, or a tracheotomy port.

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22. The method as defined in claim 18 wherein the steps of applying a voltage between the first and second current electrodes and detecting a voltage developed across the first and second sense electrodes are performed continuously.

23. The method as defined in claim 18 further comprising steps of:

providing a fluid administration system for injecting a bolus of fluid intravenously into the organism's vascular system;

periodically actuating the fluid administration system responsive to the detected voltage developed across the first and second sense electrodes.

24. The method as defined in claim 23 wherein the step of periodically actuating the fluid administration system is performed every 15 minutes only while the cardiac output is measured to be increasing.

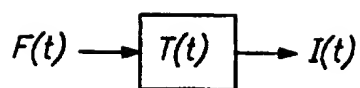
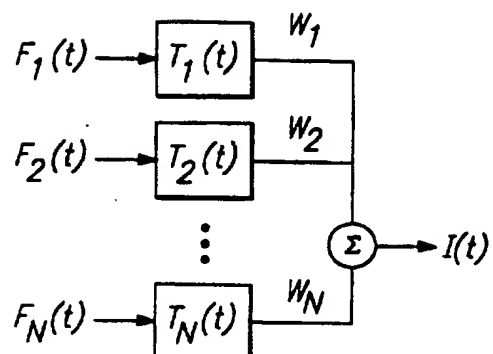
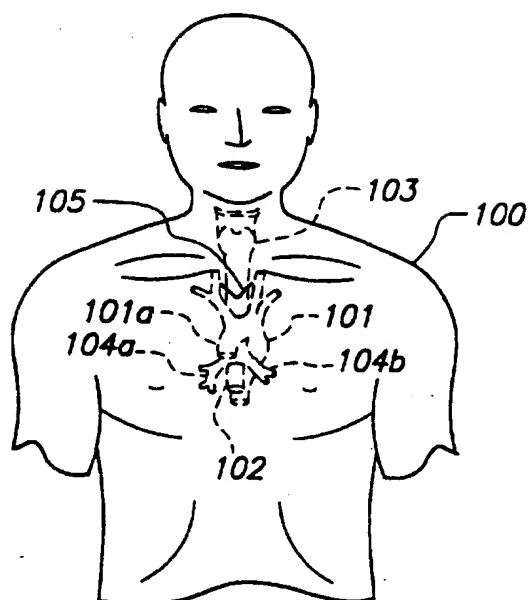
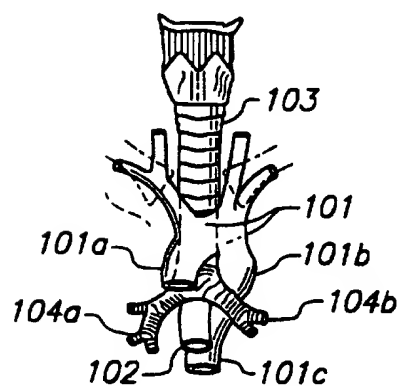
25. The method as defined in claim 18 further comprising steps of:

providing a pacemaker electrically coupled to the heart of the organism to control heart rate; and

adjusting the heart rate responsive to voltage developed across the first and second sense electrodes to optimize cardiac output.

26. The method as defined in claim 25 wherein the step of adjusting the heart rate comprises a step of lowering the heart rate to obtain either a predetermined minimum heart rate or until the cardiac output is measured to be decreasing.

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**FIG. 1A****FIG. 1B****FIG. 2A****FIG. 2B**

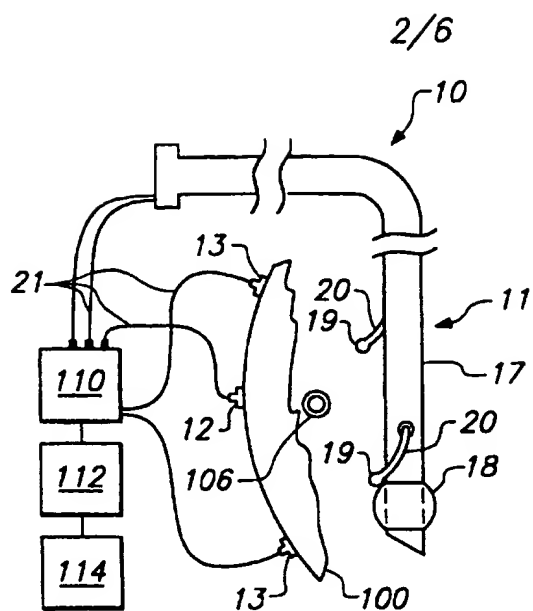


FIG. 3A

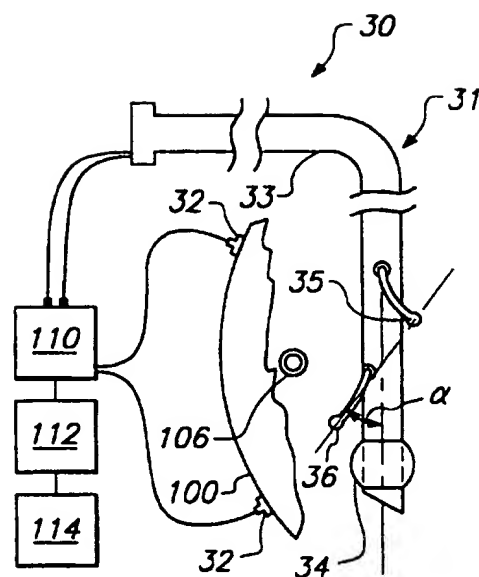


FIG. 3B

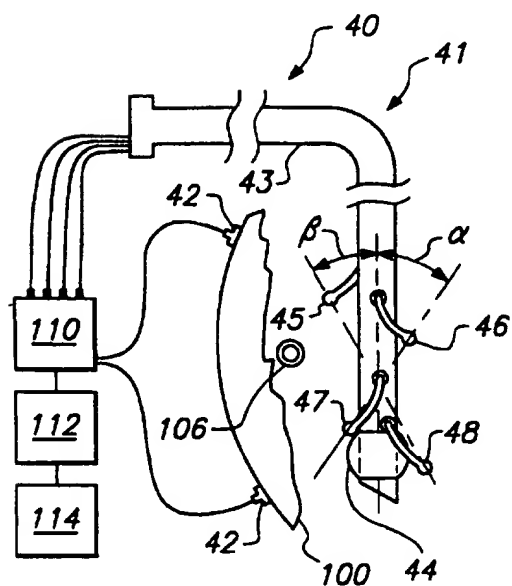


FIG. 3C

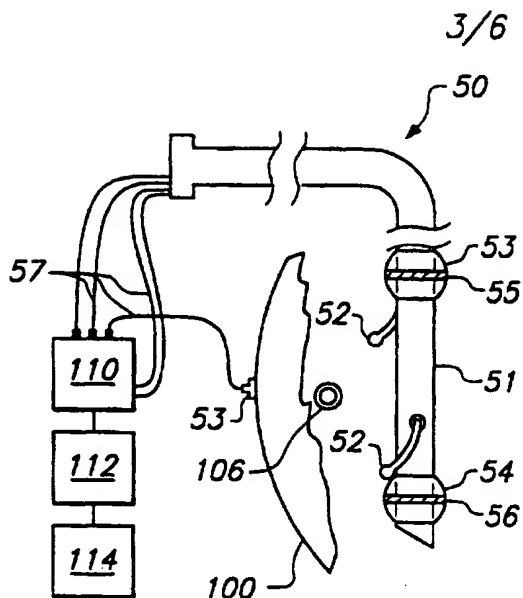


FIG. 4A

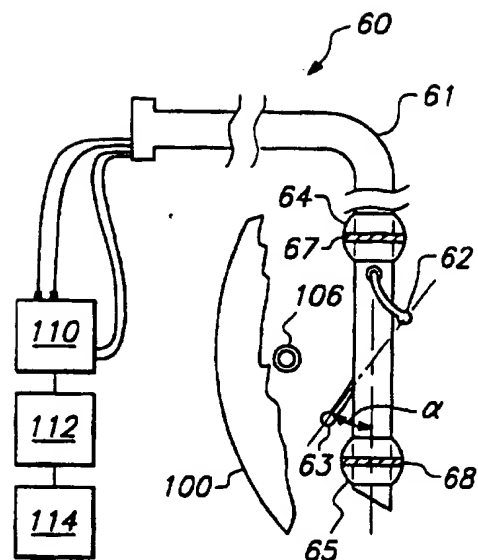


FIG. 4B

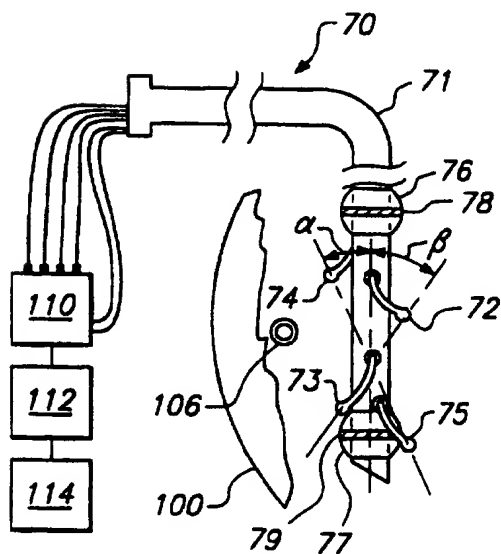


FIG. 4C

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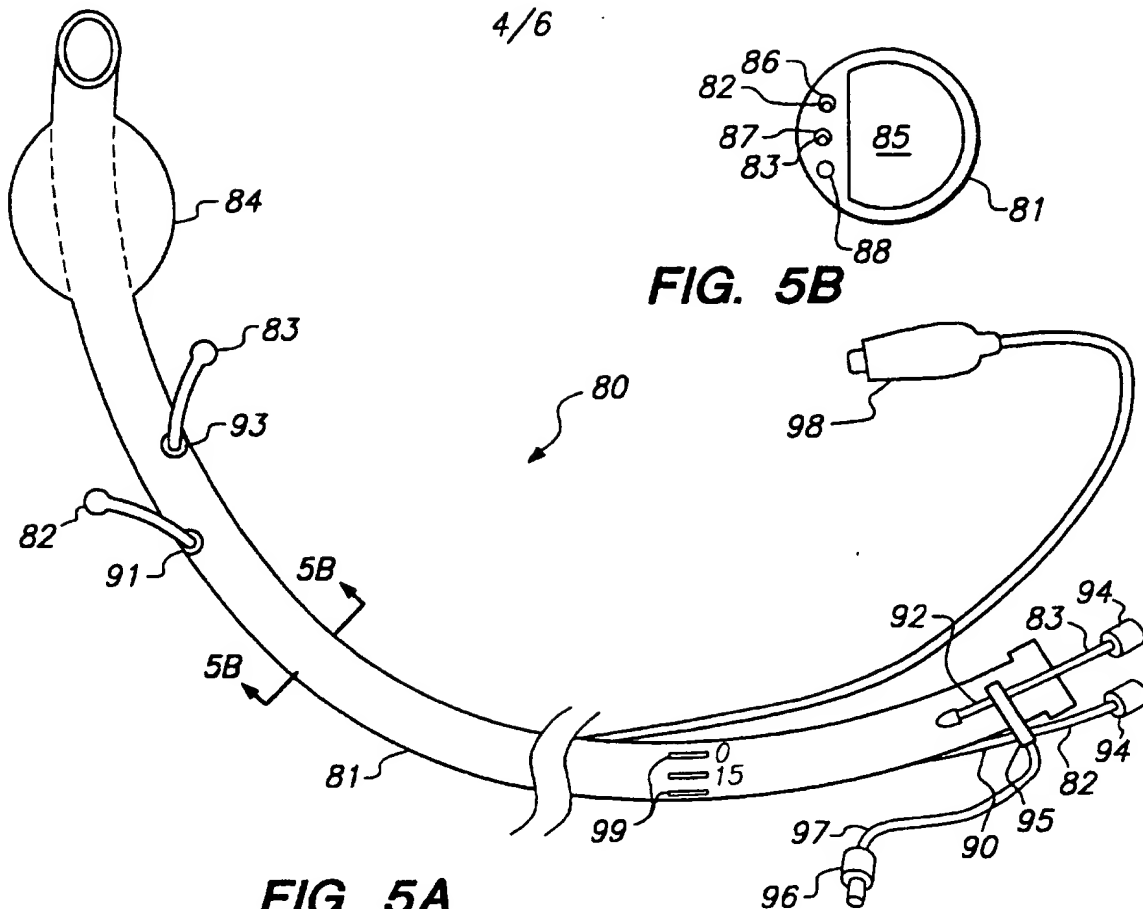


FIG. 5B

FIG. 5A

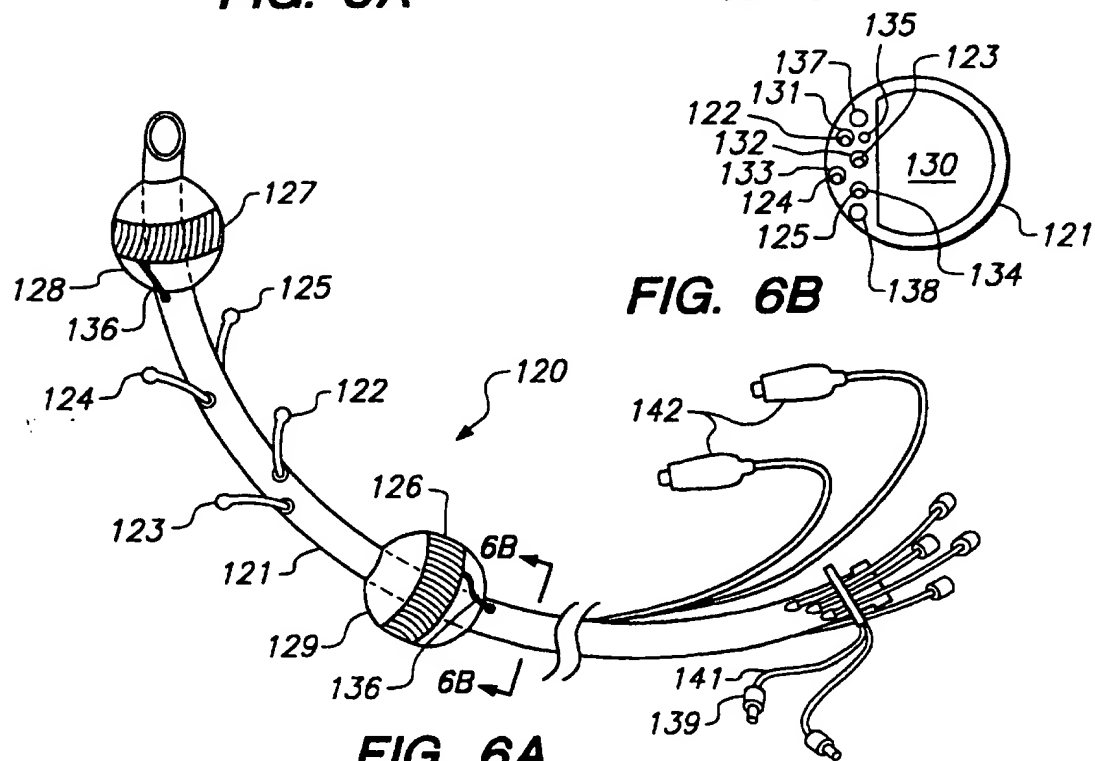
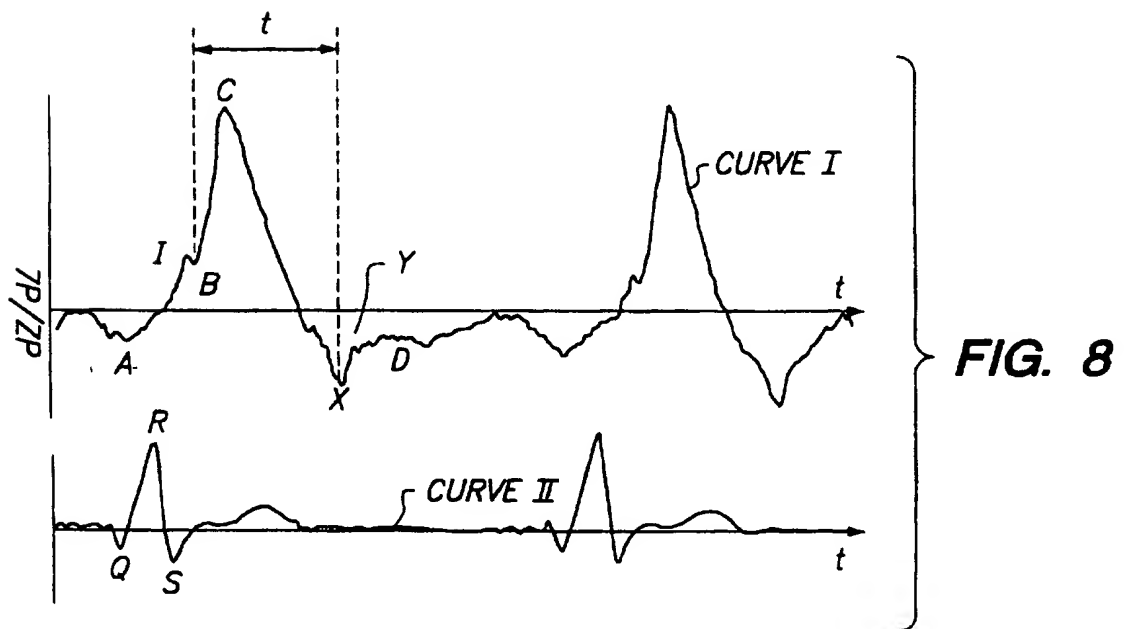
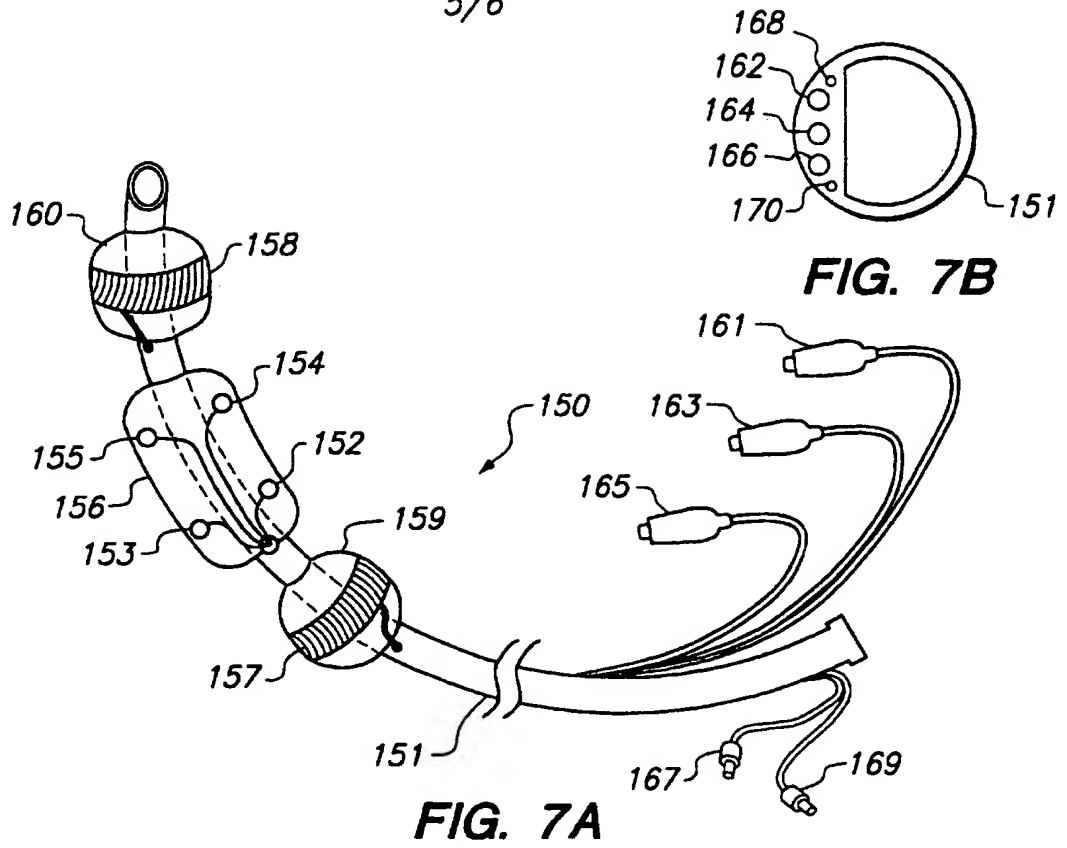


FIG. 6B

FIG. 6A

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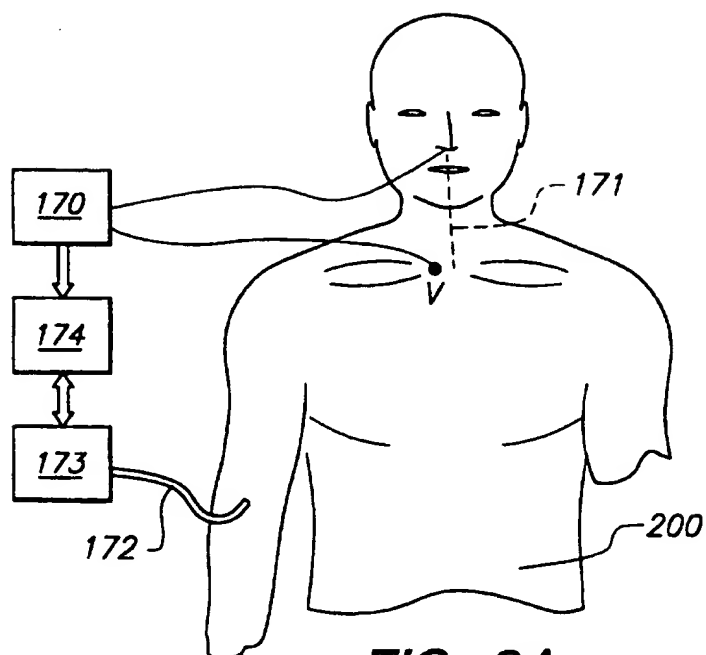


FIG. 9A

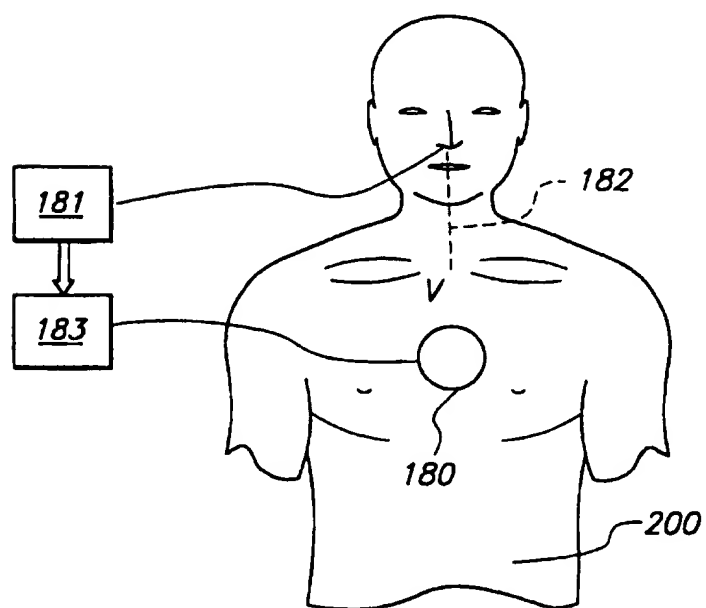


FIG. 9B

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US97/06369

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A 61 B 5/05

US CL : 128/734

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/734, 671, 635, 774

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US RE. 30101 A (KUBICEK ET AL.) 25 September 1979, col. 7, lines 20-40.	1-7, 9-15, 17-22, 25, 26
Y	US 5,379,765 A (KAJIWARA ET AL.) 10 January 1995, col. 3, lines 1-35, Fig. 4	1-7, 9-15, 17-22, 25, 26
Y	US 5,477,860 A (ESSEN-MOLLER) 26 December 1995, col. 4, lines 57-63.	15

☐ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

01 AUGUST 1997

Date of mailing of the international search report

21 AUG 1997

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